Reviewer’s report

Title: Advantages of using reduced-volume intensity modulated radiation therapy for the treatment of nasopharyngeal carcinoma: a retrospective paired study

Version: 0 Date: 07 Jan 2019

Reviewer: Christoph Süß

Reviewer’s report:

The authors present a retrospective study, comparing reduced-volume intensity modulated radiation therapy (RV-IMRT) and conventional-volume intensity modulated radiation therapy (CV-IMRT) for the treatment of nasopharyngeal carcinoma.

The article deals with an interesting topic concerning volume de-escalation in patients with nasopharyngeal carcinoma by using modern radiotherapy techniques.

However, this manuscript has some limitations. Despite those limitations, the article might be suitable for "BMC Cancer" after some revisions.

Major compulsory revision:

1) One main limitation is -as the authors themselves declare- that in this retrospective trial there is "a small amount of patients " (Line 332). In the matched pair analysis the patients are well distributed, however the applicability for the general population should be discussed critically.

2) The follow-up time was 50 months for the RV-IMRT arm. Thus long term survival condition is not available for analysis. Overall, in nasopharyngeal carcinoma the prognosis is good, which indicates that disparity in overall survival will display after a longer period of time.

3) Late toxicity is only (once) evaluated after 3 months. (page 7, Zeile 151) Is this correct? The authors should critically discuss this fact.

Why is there no evaluation of late toxicity after 6 or 12 months in spite of a median follow-up of 70 months? (Table 4, page 13) -> The main statement that "the RV-IMRT was associated with significantly reduced risk of late xerostomia … and hearing loss…” should be reevaluated after 6 or 12 months.

Minor essential revisions:
1) The authors do not describe the doses of chemotherapies which are applied nor the application days of the cycles (Page 7, lines 140-142, Page 9, line 190).

2) The authors should mention if an MRI scan or PET scan was used for delineation of the target volumes.

3) The authors should describe which organs at risk were delineated as critical structures. They only declare that the RTOG protocol was used (Page 6, line 132; Page 7, line 133). Perhaps the authors should demonstrate in a table which organs at risk were classified as critical structures.

4) On page 3, line 52 there is a typing error: ...(that) shows....

5) "LV-IMRT arm". (Page 6, line 117) Is this a typing error?

6) The patients included in this study present with stage II-IVb (page 7, line 139) respectively I,II,III and IV (page 9, line 189). The authors should critically discuss the limited validity in this broad spectrum.

7) The authors should critically discuss the limitation of the propensity score matching method (page 8, line 157)

8) In the multivariate COX regression analysis for prognostic factors only the age showed a high risk ratio for OS (page 13, line 247). Is this correct?

9) In this study the tolerability and the toxicity of chemotherapy is not investigated. Which toxicity is associated to chemotherapy? The authors should eliminate the cases with chemotherapy-associated toxicity when indicated because they falsify the comparison of RV-IMRT to CV-IMRT.

10) Did all the patients receive the same radiation concept? (33x 2,12Gy (70Gy) PTVs of GTV-P, GTV-N, 33x1,82Gy (60Gy) PTV of CTV1,33x1,7Gy (56Gy) of the PTV of CTV-2)

How many patients did receive a lower dose? If patients did receive less than 60Gy total dose, was it converted to the biologic equivalent dose?

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

No

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

No
Are the conclusions drawn adequately supported by the data shown?  
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?  
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I recommend additional statistical review

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